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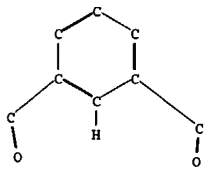
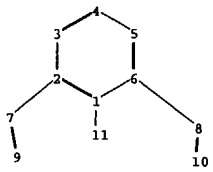




chain nodes :
7 8 9 10 11
ring nodes :
1 2 3 4 5 6
chain bonds :
1-11 2-7 6-8 7-9 8-10
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
7-9 8-10
exact bonds :
1-11 2-7 6-8
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:380438 CAPLUS
DOCUMENT NUMBER: 135:24657
TITLE: Selective cellular targeting: multifunctional delivery vehicles
INVENTOR(S): Glazier, Arnold
PATENT ASSIGNEE(S): Drug Innovation & Design, Inc., USA
SOURCE: PCT Int. Appl., 981 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001036003 | A2 | 20010525 | WO 2000-US31262 | 20001114 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2001016075 | A5 | 20010530 | AU 2001-16075 | 20001114 <-- |
| EP 1255567 | A1 | 20021113 | EP 2000-978631 | 20001114 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| US 2003138432 | A1 | 20030724 | US 2000-738625 | 20001215 |

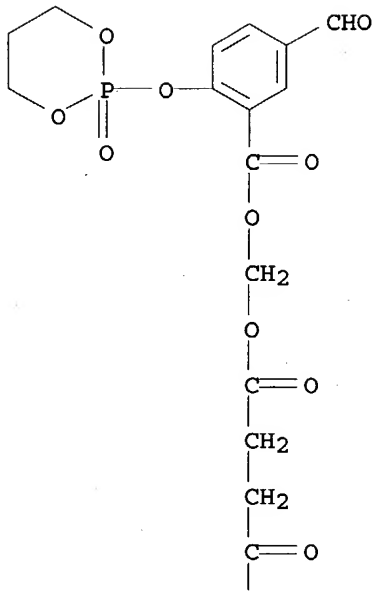
PRIORITY APPLN. INFO.:
US 1999-165485P P 19991115
US 2000-239478P P 20001011
US 2000-241937P P 20001020
WO 2000-US31262 W 20001114
US 2000-712465 B1 20001115

AB The present invention relates to the compns., methods, and applications of a novel approach to selective cellular targeting. The purpose of this invention is to enable the selective delivery and/or selective activation of effector mols. to target cells for diagnostic or therapeutic purposes. The present invention relates to multi-functional prodrugs or targeting vehicles wherein each functionality is capable of enhancing targeting selectivity, affinity, intracellular transport, activation or detoxification. The present invention also relates to ultralow dose, multiple target, multiple drug chemotherapy and targeted immunotherapy for cancer treatment.

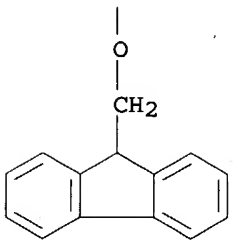
IT **341551-64-2P 341551-65-3P 341551-67-5P**
**341551-68-6P 341551-75-5P 341552-54-3P**
RL: PNU (Preparation, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(multifunctional delivery vehicles for selective cellular targeting of drugs)

RN 341551-64-2 CAPLUS
CN Butanedioic acid, 9H-fluoren-9-ylmethyl [[5-formyl-2-[(2-oxido-1,3,2-dioxaphosphorinan-2-yl)oxy]benzoyl]oxy]methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

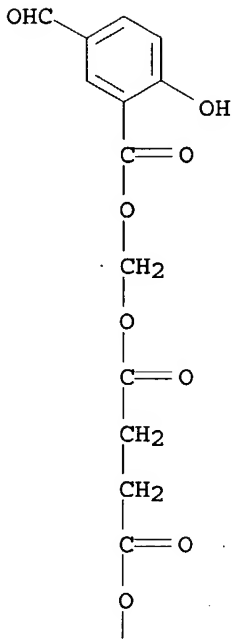


PAGE 2-A

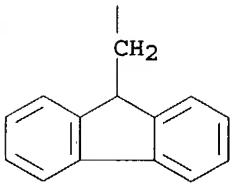


RN 341551-65-3 CAPLUS
CN Butanedioic acid, 9H-fluoren-9-ylmethyl [(5-formyl-2-hydroxybenzoyl)oxy]methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



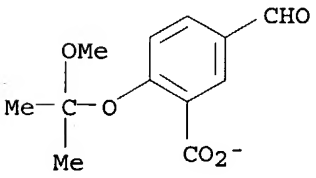
PAGE 2-A



RN 341551-67-5 CAPLUS
CN Ethanaminium, N,N,N-triethyl-, salt with 5-formyl-2-(1-methoxy-1-methylethoxy)benzoic acid (1:1) (9CI) (CA INDEX NAME)

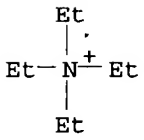
CM 1

CRN 341551-66-4
CMF C12 H13 O5

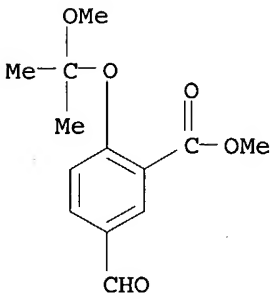


CM 2

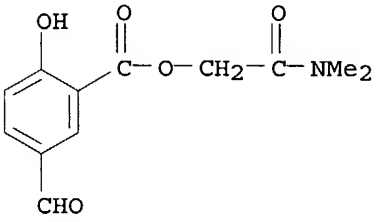
CRN 66-40-0
CMF C8 H20 N



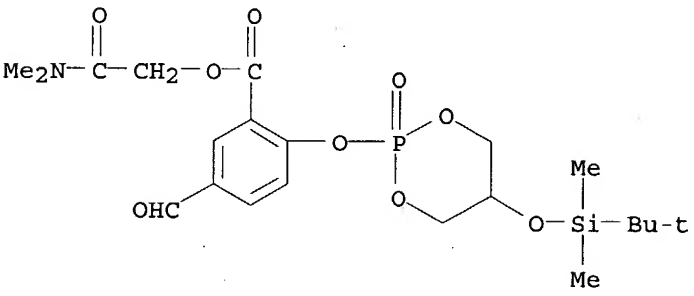
RN 341551-68-6 CAPLUS
CN Benzoic acid, 5-formyl-2-(1-methoxy-1-methylethoxy)-, methyl ester (9CI) (CA INDEX NAME)



RN 341551-75-5 CAPLUS
CN Benzoic acid, 5-formyl-2-hydroxy-, 2-(dimethylamino)-2-oxoethyl ester (9CI) (CA INDEX NAME)



RN 341552-54-3 CAPLUS
CN Benzoic acid, 2-[[5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-oxido-1,3,2-dioxaphosphorinan-2-yl]oxy]-5-formyl-, 2-(dimethylamino)-2-oxoethyl ester (9CI) (CA INDEX NAME)



L7 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:61843 CAPLUS
DOCUMENT NUMBER: 134:260866
TITLE: Identification of a novel class of small-molecule antiangiogenic agents through the screening of combinatorial libraries which function by inhibiting the binding and localization of proteinase MMP2 to integrin αVβ3
AUTHOR(S): Boger, Dale L.; Goldberg, Joel; Silletti, Steve; Kessler, Torsten; Cheresh, David A.

CORPORATE SOURCE: Departments of Chemistry Immunology and Vascular Biology, The Skaggs Institute for Chemical Biology The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Journal of the American Chemical Society (**2001**), 123(7), 1280-1288
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:260866

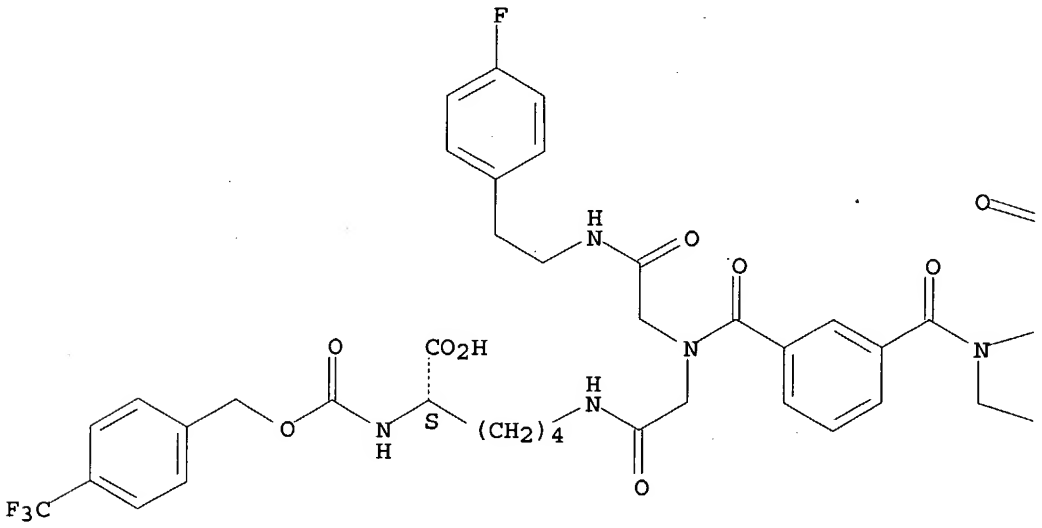
AB The process of new blood vessel growth from existing vasculature, known as angiogenesis, is critical to several pathol. conditions, most notably cancer. Both MMP2, which degrades the extracellular matrix (ECM), and integrin αVβ3, which contributes to endothelial cell attachment to the ECM, are critically involved in this process. Recent findings have shown that MMP2 is localized in an active form on the surface of invasive endothelial cells based on its ability to directly bind integrin αVβ3, suggesting that disrupting this protein-protein interaction may represent a new target for the development of angiogenesis inhibitors. The screening of small mol. libraries led to the identification of compds. which disrupt the MMP2-αVβ3 interaction in an in vitro binding assay. A prototypical inhibitor was further found to prevent the degradation of the protein matrix without directly inhibiting MMP2 activity or disrupting the binding of αVβ3 to its classical ECM ligand, vitronectin. The synthesis and screening of analogs and substructures of this lead compound allowed the identification of requisite structural features for inhibition of MMP2 binding to αVβ3. This led to the synthesis of a more water-soluble derivative which maintains the in vitro biol. properties and has potent antiangiogenic and antitumor activity in vivo, validating the target as one useful for therapeutic intervention.

IT **331714-07-9P 331714-10-4P 331714-16-0P**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(identification of novel class of small-mol. antiangiogenic agents through screening of combinatorial libraries)

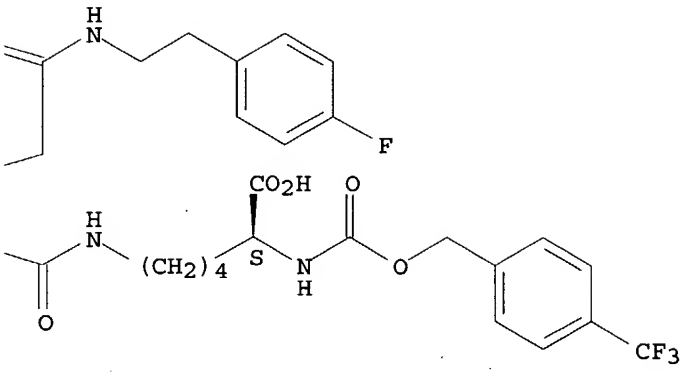
RN 331714-07-9 CAPLUS
CN L-Lysine, 1,1'-(1,3-phenylenedicarbonyl)bis[N6-[N-[2-[[2-(4-fluorophenyl)ethyl]amino]-2-oxoethyl]glycyl]-N2-[[[4-(trifluoromethyl)phenyl]methoxy]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



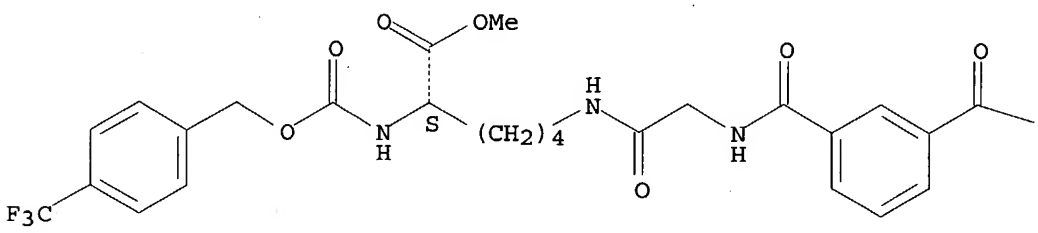
PAGE 1-B



RN 331714-10-4 CAPLUS
CN L-Lysine, N6,N6'-[1,3-phenylenebis[carbonylimino(1-oxo-2,1-ethanediyl)]]bis[N2-[[[4-(trifluoromethyl)phenyl]methoxy]carbonyl]-, dimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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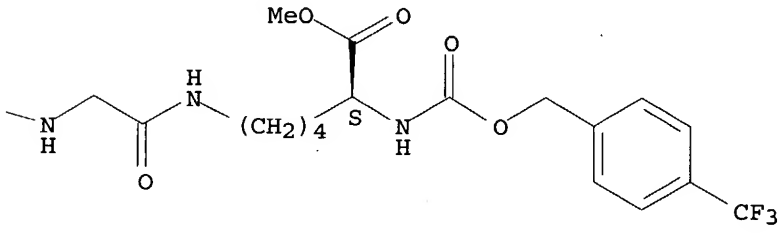


L7 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:456916 CAPLUS
DOCUMENT NUMBER: 133:68929
TITLE: Use of a matrix **metalloproteinase** inhibitor and an integrin antagonist in the treatment of neoplasia
INVENTOR(S): McKearn, John P.; Gordon, Gary; Cunningham, James J.; Gately, Stephen T.; Koki, Alane T.; Masferrer, Jaime L.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 358 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 19
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000038719 | A1 | 20000706 | WO 1999-US30700 | 19991222 <-- |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2356402 | AA | 20000706 | CA 1999-2356402 | 19991222 <-- |
| EP 1140183 | A1 | 20011010 | EP 1999-968942 | 19991222 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2002533407 | T2 | 20021008 | JP 2000-590670 | 19991222 |
| ZA 2001005055 | A | 20020920 | ZA 2001-5055 | 20010620 |
| ZA 2001005120 | A | 20020107 | ZA 2001-5120 | 20010621 |

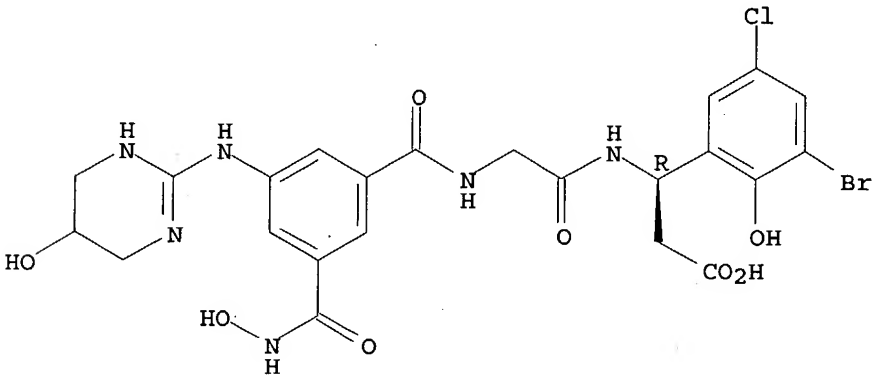
PRIORITY APPLN. INFO.: US 1998-113786P P 19981223
WO 1999-US30700 W 19991222

AB Methods are provided to treat or prevent neoplasia disorders in a mammal using a combination of a matrix **metalloproteinase** inhibitor, an integrin antagonist, and an antineoplastic agent.

IT **280105-14-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(matrix **metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)

RN 280105-14-8 CAPLUS
CN β-Alanine, N-[3-[(hydroxyamino)carbonyl]-5-[(1,4,5,6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:335229 CAPLUS
DOCUMENT NUMBER: 132:343358
TITLE: Cystine derivatives as therapeutic agents for matrix metalloprotease-related diseases
INVENTOR(S): Grams, Frank; Krell, Hans-Willi; Leinert, Herbert; Zimmermann, Gerd
PATENT ASSIGNEE(S): Roche Diagnostics G.m.b.H., Germany
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000027378 | A2 | 20000518 | WO 1999-EP8460 | 19991105 <-- |
| WO 2000027378 | A3 | 20010920 | | |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| BR 9915127 | A | 20010731 | BR 1999-15127 | 19991105 <-- |
| EP 1143960 | A2 | 20011017 | EP 1999-971709 | 19991105 <-- |
| EP 1143960 | A3 | 20011205 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2002529404 | T2 | 20020910 | JP 2000-580607 | 19991105 |
| ZA 2001003605 | A | 20011211 | ZA 2001-3605 | 20010504 <-- |

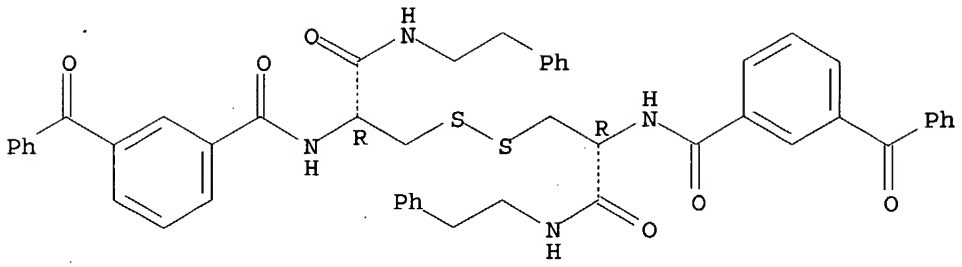
PRIORITY APPLN. INFO.: EP 1998-121073 A 19981106
WO 1999-EP8460 W 19991105
OTHER SOURCE(S): MARPAT 132:343358

AB Pharmaceutical compns. are disclosed which contain nonpeptidic cystine derivs. R1ANHCH[CH2SSCH2CH(R3ANH)(C(O)NHR4)]C(O)NHR2 [R1, R3 = H, (non)aromatic carbocyclic or heterocyclic ring, (un)branched (un)saturated C1-15 alkyl which can be interrupted by hetero atom and which can be substituted by (non)aromatic carbocyclic or heterocyclic ring; R2, R4 = H, (un)branched (un)saturated C1-15 alkyl which can be interrupted by hetero atom and which can be substituted by (non)aromatic carbocyclic or heterocyclic ring; A = valency bond, CO, SO2, NHCO, NHCS or OC(O)], their pharmacol. acceptable salts and optically active forms thereof and pharmaceutically acceptable carriers, for the treatment of diseases selected from tumor growth and metastasis; inflammatory diseases, e.g. osteo- and rheumatoid arthritis; osteoporosis; multiple sclerosis; periodontitis; restenosis; diseases caused by bacteria, e.g. meningitis; sun-induced skin aging; and Alzheimer's disease. New compds. are also disclosed.

IT **269067-09-6P 269067-10-9P 269067-11-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cystine derivative for treatment of matrix metalloprotease-related disease)

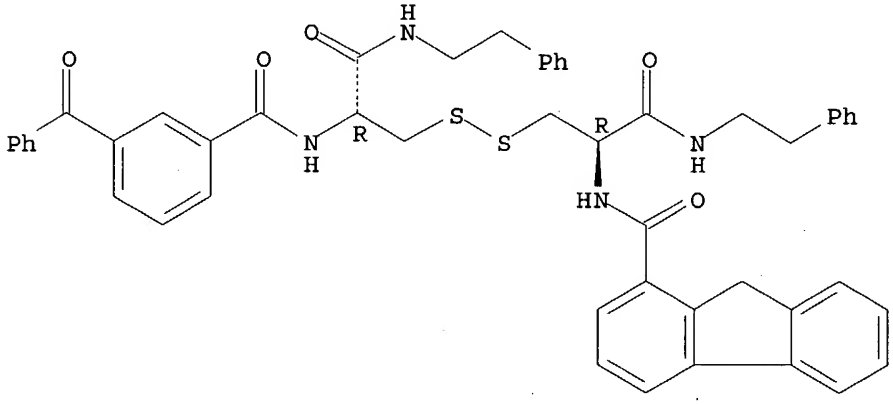
RN 269067-09-6 CAPLUS
CN Benzamide, N,N'-[dithiobis[(1R)-1-[[(2-phenylethyl)amino]carbonyl]-2,1-ethanediyl]]bis[3-benzoyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



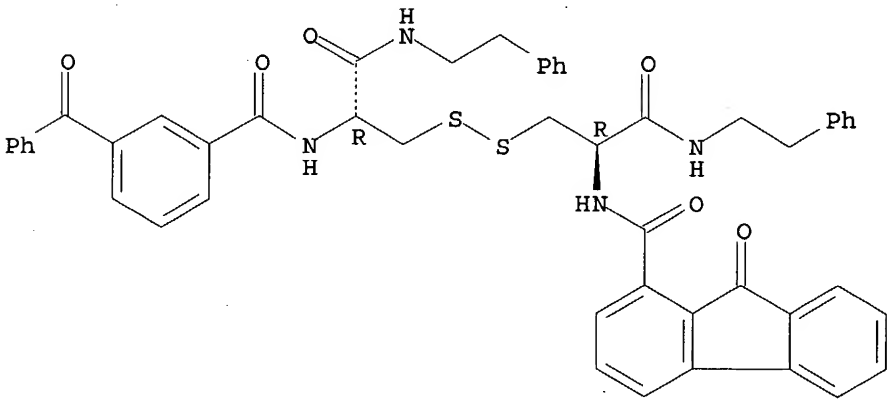
RN 269067-10-9 CAPLUS
CN 9H-Fluorene-1-carboxamide, N-[(1R)-1-[[[(2R)-2-[(3-benzoylbenzoyl)amino]-3-oxo-3-[(2-phenylethyl)amino]propyl]dithio]methyl]-2-oxo-2-[(2-phenylethyl)amino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 269067-11-0 CAPLUS
CN 9H-Fluorene-1-carboxamide, N-[(1R)-1-[[[(2R)-2-[(3-benzoylbenzoyl)amino]-3-oxo-3-[(2-phenylethyl)amino]propyl]dithio]methyl]-2-oxo-2-[(2-phenylethyl)amino]ethyl]-9-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:495123 CAPLUS
DOCUMENT NUMBER: 131:129760
TITLE: Preparation of sulfonamidobenzenehydroxamates and analogs as matrix **metalloproteinase** and TACE inhibitors
INVENTOR(S): Levin, Jeremy Ian; Du, Mila T.; Venkatesan, Aranapakam Mudumbai; Nelson, Frances Christy; Zask, Arie; Gu, Yansong
PATENT ASSIGNEE(S): American Cyanamid Co., USA

SOURCE: U.S., 68 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

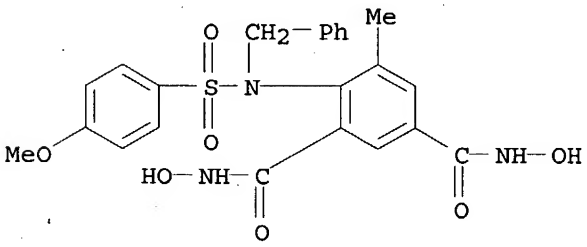
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5929097 | A | 19990727 | US 1997-944593 | 19971006 <-- |

PRIORITY APPLN. INFO.: US 1996-28504P P 19961016
OTHER SOURCE(S): MARPAT 131:129760

AB RSO2N(CH2R7)ZCONHOH [I; R = (un)substituted (hetero)aryl; R7 = H, alkyl, Ph, etc.; Z = (un)substituted phenylene or -naphthylene] were prepared Thus, 2-(H2N)C6H4CO2Me was amidated by 4-(MeO)C6H4SO2Cl and the N-benzylated product converted in 2 steps to I [R = C6H4(OMe)-4, R7 = Ph, Z = 1,2-phenylene]. Data for biol. activity of I were given.

IT **206549-45-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of sulfonamidobenzenehydroxamates and analogs as matrix **metalloproteinase** and TACE inhibitors)

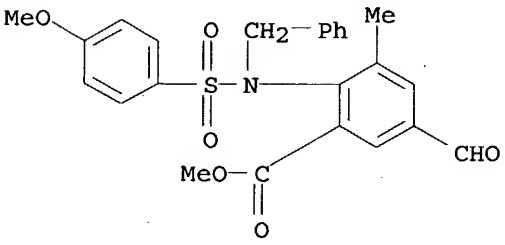
RN 206549-45-3 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-dihydroxy-4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-5-methyl-, disodium salt (9CI) (CA INDEX NAME)



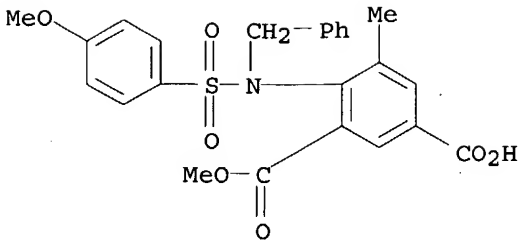

●2 Na

IT **206549-41-9P 206549-42-0P 206549-43-1P**
**206549-44-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of sulfonamidobenzenehydroxamates and analogs as matrix **metalloproteinase** and TACE inhibitors)

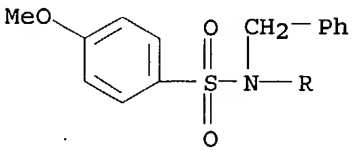
RN 206549-41-9 CAPLUS
CN Benzoic acid, 5-formyl-2-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-3-methyl-, methyl ester (9CI) (CA INDEX NAME)

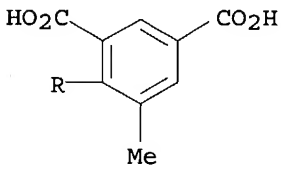



RN 206549-42-0 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-5-methyl-, 3-methyl ester (9CI) (CA INDEX NAME)

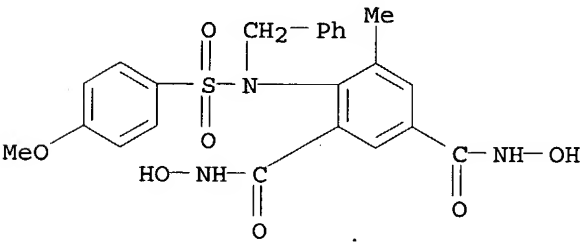


RN 206549-43-1 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-5-methyl- (9CI) (CA INDEX NAME)





RN 206549-44-2 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-dihydroxy-4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-5-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:96248 CAPLUS
DOCUMENT NUMBER: 130:148689
TITLE: Phosphonated agents and their antiangiogenic and antitumorigenic use
INVENTOR(S): Collins, Delwood C.; Gagliardi, Antonio R.; Nickel, Peter
PATENT ASSIGNEE(S): University of Kentucky Research Foundation, USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9905148 | A1 | 19990204 | WO 1998-US15470 | 19980724 <-- |
| W: AU, CA, JP, MX | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| AU 9885915 | A1 | 19990216 | AU 1998-85915 | 19980724 <-- |
| AU 739637 | B2 | 20011018 | | |
| EP 1019419 | A1 | 20000719 | EP 1998-937133 | 19980724 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |

PRIORITY APPLN. INFO.: US 1997-899996 A 19970724
WO 1998-US15470 W 19980724

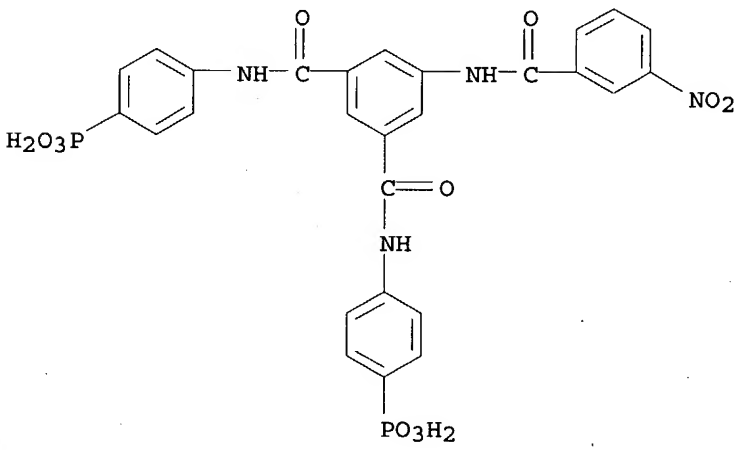
OTHER SOURCE(S): MARPAT 130:148689

AB The present invention relates to novel phosphonic acid substituted agents and their pharmaceutical compns. Phosphonic acid substituted agents that are potent inhibitors of angiogenesis or tumorigenesis is defined by the following formula: (P-Yn1)m1-Q1-K-(Q2-(Yn2-P)m2)j (P = phosphonic group, phosphonic salt; Y = OCO, NR1CO, CON(R1)R2; Q1, Q2 = aryl; K = H, NHCONH, NHCSNH, NHCOR3, NHCSR3CSNH; j, n1, n2 = 0-2; m1, m2 = 1-4; R1 = H, CH2CO2H, alkyl; R2 = alkyl, aryl, alkaryl; R3 = aryl). A pharmaceutical composition for the treatment of angiogenesis-dependent conditions or tumors comprises an effective amount of a phosphonic acid agent and a pharmaceutically acceptable carrier. Some of the phosphonic acid agents were more potent inhibitors of angiogenesis in the chick chorioallantoic membrane (CAM) assay and to human microvascular endothelial cell growth than suramin.

IT **220240-01-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphonic acid agents and their antiangiogenic and antitumorigenic use)

RN 220240-01-7 CAPLUS

CN Phosphonic acid, [[5-[(3-nitrobenzoyl)amino]-1,3-phenylene]bis(carbonylimino-4,1-phenylene)]bis-, disodium salt (9CI) (CA INDEX NAME)




●2 Na

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:747616 CAPLUS
DOCUMENT NUMBER: 130:11982
TITLE: Fluorogenic protease substrates based on dye-dimerization

INVENTOR(S): Wei, Ai-Ping; Williams, Michael G.
PATENT ASSIGNEE(S): Minnesota Mining and Manufacturing Co., USA
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9850579 | A1 | 19981112 | WO 1997-US16579 | 19970908 <-- |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9743550 | A1 | 19981127 | AU 1997-43550 | 19970908 <-- |
| EP 980440 | A1 | 20000223 | EP 1997-941691 | 19970908 <-- |
| R: CH, DE, FR, GB, IT, LI, SE | | | | |
| CN 1254383 | A | 20000524 | CN 1997-182147 | 19970908 <-- |
| JP 2002506343 | T2 | 20020226 | JP 1998-548022 | 19970908 |

PRIORITY APPLN. INFO.: US 1997-846828 A 19970501
WO 1997-US16579 W 19970908

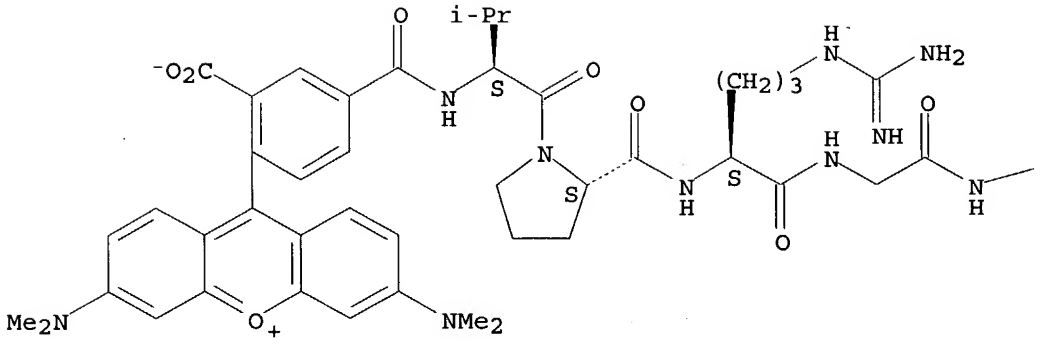
AB A method of biol. assay comprises the steps of providing an enzyme substrate comprising 2 fluorescence dye groups bound to a peptide, the dye groups being of proximity sufficiently close so as to essentially self-quench fluorescence of the dye groups, wherein self-quenching of fluorescence of the dye groups is effected by dye stacking, and enzymically cleaving the peptide to release the fluorescence dye groups from dye stacking, and producing an increase in fluorescence intensity. A protease substrate I (TMR-Val-Pro-Arg-Gly-Lys-TMR, TMR = tetramethylrhodamine) for use in the method of the invention is also disclosed. For a wide spectrum of excitation frequencies, fluorescence intensity of the cleaved substrate solution is as much as 29-fold that of the intact substrate solution, averaging from 25-28-fold the intensity, for emission wavelengths from 570 to 585 nm, a range easily visible to the human eye. This invention finds use in detection and identification of microorganisms, sterilization assurance, pharmaceutical discovery, enzyme assays, immunoassays, and other biol. assays. Use of the fluorogenic protease substrate I is demonstrated for the detection of Vibrio parahaemolyticus.

IT **216006-99-4**
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(fluorogenic protease substrates based on dye-dimerization)

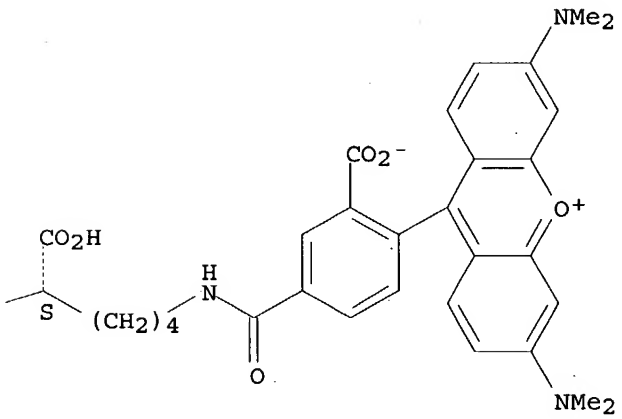
RN 216006-99-4 CAPLUS

CN L-Lysine, N-[3-carboxy-4-[3,6-bis(dimethylamino)xanthylium-9-yl]benzoyl]-L-valyl-L-prolyl-L-arginylglycyl-N6-[3-carboxy-4-[3,6-bis(dimethylamino)xanthylium-9-yl]benzoyl]-, bis(inner salt) (9CI) (CA INDEX NAME)

Absolute stereochemistry.







REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:251153 CAPLUS
DOCUMENT NUMBER: 128:308308
TITLE: The preparation and use of ortho-sulfonamido aryl hydroxamic acids as matrix **metalloproteinase** and TACE inhibitors
INVENTOR(S): Levin, Jeremy Ian; Du Mila, T.; Venkatesan, Aranapakam Mudumbai; Nelson, Frances Christy; Zask, Arie; Gu, Yansong
PATENT ASSIGNEE(S): American Cyanamid Company, USA
SOURCE: PCT Int. Appl., 164 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9816503 | A2 | 19980423 | WO 1997-US18280 | 19971008 <-- |

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ,

VN, YU, ZW
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

| | | | | | |
|---|---|---|---|---|---|
| AU 9851458 | A1 | 19980511 | AU 1998-51458 | 19971008 | <-- |
| AU 731737 | B2 | 20010405 | | | |
| EP 938471 | A1 | 19990901 | EP 1997-946246 | 19971008 | <-- |
| EP 938471 | B1 | 20011212 | | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO | | | | | |
| BR 9712525 | A | 19991019 | BR 1997-12525 | 19971008 | <-- |
| CN 1240429 | A | 20000105 | CN 1997-180613 | 19971008 | <-- |
| JP 2001504809 | T2 | 20010410 | JP 1998-518448 | 19971008 | <-- |
| AT 210637 | E | 20011215 | AT 1997-946246 | 19971008 | <-- |
| ES 2166102 | T3 | 20020401 | ES 1997-946246 | 19971008 | |
| PT 938471 | T | 20020531 | PT 1997-97946246 | 19971008 | |
| ZA 9709233 | A | 19990415 | ZA 1997-9233 | 19971015 | <-- |
| TW 410220 | B | 20001101 | TW 1997-86114187 | 19971015 | <-- |
| KR 2000049196 | A | 20000725 | KR 1999-703294 | 19990415 | <-- |
| HK 1021178 | A1 | 20020404 | HK 2000-100090 | 20000106 | |

PRIORITY APPLN. INFO.: US 1996-732631 A 19961016
WO 1997-US18280 W 19971008

OTHER SOURCE(S): MARPAT 128:308308

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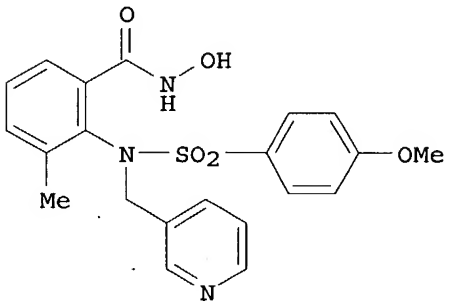


II